PATENT COOPERATION TREATY

| | From the INTERNATIONAL BUREAU |
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| PCT | То: |
| NOTIFICATION OF ELECTION (PCT Rule 61.2) | United States Patent and Trademark Office (Box PCT) Crystal Plaza 2 Washington, DC 20231 ÉTATS-UNIS D'AMÉRIQUE |
| Date of mailing (day/month/year) 08 January 1999 (08.01.99) | in its capacity as elected Office |
| International application No. PCT/GB98/01395 | Applicant's or agent's file reference M96/0693/PCT |
| International filing date (day/month/year) 22 May 1998 (22.05.98) | Priority date (day/month/year) 22 May 1997 (22.05.97) |
| Applicant FREESTONE, Primrose, Pamela, Elaine et al | |
| 1. The designated Office is hereby notified of its election made. X in the demand filed with the International Preliminary 09 December 19 | Examining Authority on: 998 (09.12.98) Itional Bureau on: |

Authorized officer

Telephone No.: (41-22) 338.83.38

P. Regis

Form PCT/IB/331 (July 1992)

Facsimile No.: (41-22) 740.14.35

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland

PATENT COOPERATION TREATY

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INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

| Applicant's | or agent's | file reference | | See Notifi | cation of Transmittal of International | |
|-------------------------|--|---|---|-------------------|---|--|
| M96/069 | 3/PCT | | FOR FURTHER ACTION | ON Preliminar | y Examination Report (Form PCT/IPEA/ | 416) |
| Internationa | al applicat | ion No. | International filing date (day/i | month/year) | Priority date (day/month/year) | |
| PCT/GB9 | 98/0139 | 5 | 22/05/1998 | | 22/05/1997 | |
| Internationa C12N1/3 | | Classification (IPC) or na | tional classification and IPC | | | |
| Applicant UNIVER | SITY OI | LEICESTER et al. | | | | |
| 1. This i | nternatio s transmi | onal preliminary exami itted to the applicant a | nation report has been pre ccording to Article 36. | pared by this In | ternational Preliminary Examining A | uthority |
| 2. This f | REPORT | consists of a total of | 5 sheets, including this co | ver sheet. | | |
| b | een ame | ended and are the bas | d by ANNEXES, i.e. sheets sis for this report and/or she of of the Administrative Ins | ets containing i | on, claims and/or drawings which hare rectifications made before this Author the PCT). | ave ority |
| These | e annexe | es consist of a total of | sheets. | | | ! |
| | _ | | ting to the following items: | | | |
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| | □ P | • | ninion with regard to novel | tv. inventive ste | p and industrial applicability | |
| IV | | ack of unity of invention | | ty, mivernive ste | p and madernal applicability | |
| v | ⊠R | easoned statement u | | | ventive step or industrial applicabilit | y; |
| VI | □с | ertain documents cite | ed | | | |
| VII | VII Certain defects in the international application | | | | | |
| VIII | | ertain observations or | n the international applicati | on | | |
| Date of sub | omission o | of the demand | D | ate of completion | of this report 2 9. 07: 99 | |
| 09/12/19 | 98 | | T | | | |
| | examinin | ddress of the international gauthority: | ıl A | uthorized officer | المالية | AGOVES MITERIORS |
| <u>)</u> | D-8029 Tel. (+4 | an Patent Office 8 Munich 19-89) 2399-0 Tx: 52365 | 6 epmu d | loonen, P | Sayan Son no A | 2) 22145 - 22145 AND |
| | Fax: (+49-89) 2399-4465 Telephone No. (+49-89) 2399 8538 | | | | | |

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/GB98/01395

| I. Bas | is of | the | re | por | t |
|--------|-------|-----|----|-----|---|
|--------|-------|-----|----|-----|---|

1. This report has been drawn on the basis of (substitute sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to the report since they do not contain amendments.): Description, pages: 1-28 as originally filed Claims, No.: 1-16 as originally filed Drawings, sheets: 1/12-12/12 as originally filed 2. The amendments have resulted in the cancellation of: ☐ the description, pages: ☐ the claims, Nos.: ☐ the drawings, sheets: 3.

This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

4. Additional observations, if necessary:

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/GB98/01395

- V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- 1. Statement

Novelty (N) Yes: Claims 1-16

No: Claims

Inventive step (IS) Yes: Claims 1-16

No: Claims

Industrial applicability (IA) Yes: Claims 1-16

No: Claims

2. Citations and explanations

see separate sheet

Reference is made to the following documents:

D1: FEMS Microbiol Lett 139 (1996) 155-9; cited in the application

D2: J Bacteriol **177** (1995) 6989-92

D3: Nature **362** (1993) 446-448; cited in the application

Introduction:

Bacterial autoinducers of growth are known from the prior art: 1.

D1 has disclosed an autoinducer from E coli having a MW of 10,000 as indicated by preliminary experiments utilizing preparative ultrafiltration.

D2 concerns different autoinducers from P aeruginosa of the homoserine lactone type.

D3 refers in Figure 2 to low molecular weight homoserine lactone derivatives containing a lipophilic acyl chain as autoinducer (also mentioned in the description; see e.g. page 1 last full paragraph).

Re Item V

Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

2. The present invention concerns the isolation of a low molecular weight autoinducer (AI) obtainable from E.coli, having a number of established properties (e.g. see Table 5 of the specification), although the chemical formula has not yet been established. The AI of the present application is differentiated from the known AI, referred to in D2-D3 as well as other obvious compounds like a known siderophore.

With respect to D1, it is noted that in the present application in step 1 (see page 13, first paragraph) the AI is bound to a factor with MW of around 10 kDa and may be separated therefrom by several procedures (e.g. heat-treatment). D1 is therefore considered to be the closest state of the art, as in D1 the complex has

INTERNATIONAL PRELIMINARY International application No. PCT/GB98/01395 EXAMINATION REPORT - SEPARATE SHEET

only be isolated.

3. An inventive step for the presently purified and characterized AI of E coli is recognised (Article 33(3) PCT). As the structure of the AI is not known, it is considered that all the properties of the AI as referred to in dependent claims 2 and 3 and including the MW <500 Da mentioned in Table 5 are essential to the invention and should be present in all the independent claim on file (including the independent claims 5 and 15); see Article 6 PCT and Rule 6.3(b) PCT. No other AI than the AI with the above mentioned essential technical features has been disclosed, i.e. it is not clearly supported by the application if the autoinducer of present claim 1 refers to a family of different autoinducers.

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INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

| Applicant's or agent's file reference | /Form PCT/ISA/2 | of Transmittal of International Search Report (20) as well as, where applicable, item 5 below. |
|--|---|---|
| M96/0693/PCT | ACTION | |
| International application No. | International filing date (day/month/year) | (Earliest) Priority Date (day/month/year) |
| PCT/GB 98/01395 | 22/05/1998 | 22/05/1997 |
| Applicant | | |
| | | |
| UNIVERSITY OF LEICESTER e | t al. | |
| This International Search Report has beer according to Article 18. A copy is being tra | n prepared by this International Searching Auth nsmitted to the International Bureau. | nority and is transmitted to the applicant |
| This International Search Report consists It is also accompanied by a copy | of a total of <u>3</u> sheets. of each prior art document cited in this report. | |
| Certain claims were found uns | searchable(see Box I). | |
| 2. Unity of invention is lacking(se | ee Box II). | |
| The international application con international search was carried | tains disclosure of a nucleotide and/or amino out on the basis of the sequence listing | acid sequence listing and the |
| | with the international application. | |
| furni | shed by the applicant separately from the inter | |
| L | but not accompanied by a statement to the matter going beyond the disclosure in the | e effect that it did not include international application as filed. |
| Tran | scribed by this Authority | |
| | ext is approved as submitted by the applicant | |
| <u></u> | ext has been established by this Authority to re | ead as follows: |
| E. COLI, SALMONELLA OR | HAFNIA AUTOINDUCERS | |
| 5. With regard to the abstract, | | |
| X the to | ext is approved as submitted by the applicant | |
| Box | ext has been established, according to Rule 38 III. The applicant may, within one month fromt ch Report, submit comments to this Authority. | 8.2(b), by this Authority as it appears in he date of mailing of this International |
| 6. The figure of the drawings to be publis | shed with the abstract is: | |
| Figure No as su | uggested by the applicant. | X None of the figures. |
| | use the applicant failed to suggest a figure. | |
| beca | use this figure better characterizes the invention | on. |



ternational Application No PCT/GB 98/01395

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|------------------------|---|--|---|
| A. CLASS IPC 6 | FICATION OF SUBJECT MATTER C12N1/38 C12P1/04 C12R1:19,C12R1:42) | 04 //(C12P1/04,C12R1 | 01, |
| According t | o International Patent Classification (IPC) or to both national classific | eation and IPC | |
| B. FIELDS | SEARCHED | | |
| Minimum de IPC 6 | ocumentation searched (classification system followed by classificat C12N C12P | on symbols) | |
| | tion searched other than minimumdocumentation to the extent that s | | rched |
| Electronic c | lata base consulted during the international search (name of data ba | ase and, where practical, search terms used) | |
| C. DOCUM | ENTS CONSIDERED TO BE RELEVANT | | |
| Category ° | Citation of document, with indication, where appropriate, of the rel | evant passages | Relevant to claim No. |
| А | LYTE M ET AL: "Production of an autoinducer of growth by noreping cultured Escherichia coli 0157:H FEMS MICROBIOL LETT, JUN 1 1996, P155-9, XP002078986 NETHERLANDS cited in the application | 7." | |
| Α | MCKENNEY D ET AL: "Influence of Pseudomonas aeruginosa exoproduction in Burkholderia cepacia: evidence of interspecies communication." J BACTERIOL, DEC 1995, 177 (23) I XP002078987 UNITED STATES | f | |
| X Furth | ner documents are listed in the continuation of box C. | Patent family members are listed in | annex. |
| ° Special ca | tegories of cited documents : | OTTO Johan da surre de la Colonia de la Colo | |
| consid E" earlier o | ent defining the general state of the art which is not ered to be of particular relevance locument but published on or after the international | "T" later document published after the intern or priority date and not in conflict with the cited to understand the principle or the invention "X" document of particular relevance; the classification | ne application but ory underlying the |
| which i | ate nt which may throw doubts on priority claim(s) or is cited to establish the publication date of another n or other special reason (as specified) | cannot be considered novel or cannot be involve an inventive step when the docurer of particular relevance; the clacannot be considered to involve an inventive and invent | e considered to Iment is taken alone Imed invention |
| other n | int published prior to the international filing date but | document is combined with one or more ments, such combination being obvious in the art. | e other such docu- to a person skilled |
| | an the priority date claimed | "&" document member of the same patent fa Date of mailing of the international search | |
| 29 | 9 September 1998 | 12/10/1998 | |
| Name and m | nailing address of the ISA European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, | Authorized officer | |

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| ategory ° | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
|-----------|---|-----------------------|
| | ZHANG L ET AL: "Agrobacterium conjugation and gene regulation by N-acyl-L-homoserine lactones" NATURE, vol. 362, 1993, pages 446-448, XP002078988 LONDON GB | |
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